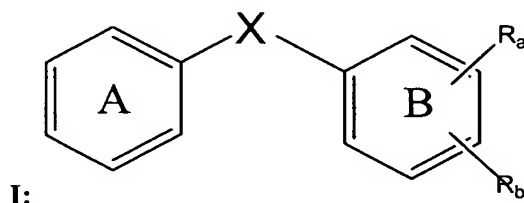


CLAIMS

What is claimed is:

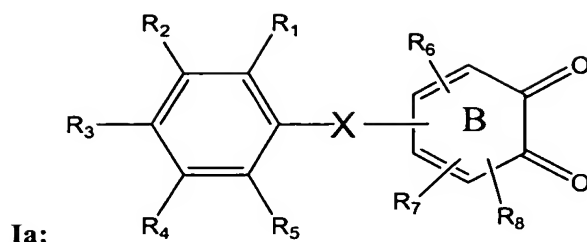
1. A composition which selectively reduces blood flow to a tumor region and forms a
 5 ROS *in vivo*, wherein said composition comprises an anticancer agent having a quinone, quinone prodrug, catechol or catechol prodrug moiety, provided that said composition is not combretastatin A-1 or a salt, ester or prodrug thereof.
2. The composition of claim 1 wherein said moiety is in the *ortho* position.
3. The composition of claim 1 wherein said anticancer agent is a tubulin binding agent.
- 10 4. A compound comprising the structure of formula I:



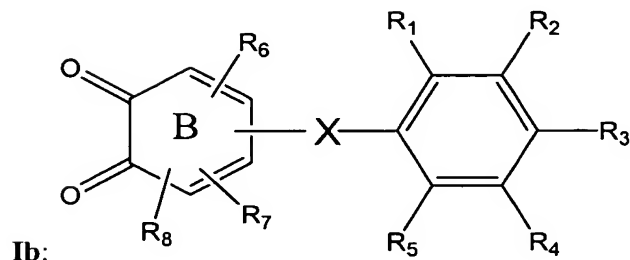
wherein:

- Ring A is optionally substituted with one to five substituents selected from
 - 15 a) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - b) a halogen or trihaloalkyl;
 - c) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - 20 d) an OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 - e) NH₂ or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or

- f) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;
- 5 - Ring B comprises at least one structure denoted by R_a and R_b , which represent an *ortho*-quinone moiety $-(C=O)-(C=O)-$, *ortho*-catechol moiety $-(C-OH)-(C-OH)-$ or *ortho*-catechol pro-drug moiety $-(C-O-Prodrug\ moiety)-(C-O-Prodrug\ moiety)-$; and the remaining carbons of Ring B are optionally substituted with one to five substituents selected from
- g) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
- 10 h) a halogen or trihaloalkyl;
- i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
- j) OH or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;
- 15 k) NH_2 or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
- l) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
- 20 - Bridge X is selected from the group consisting of alkenes $-(CR_9=CR_{10})-$, alkanes $-(CR_9-CR_{11}R_{12})$, alkynes, amides $-(NR_9-CO)-$, amines $-(NH-$, $-NR_8-$, or $-CR_9-N-$), carbonyl $-(CO)-$, ethers $-(C\ R_8-O)-$, sulfonamides $-(NR_8-SO_2)-$, sulfonates $-(O-SO_2)-$, aryls, oxo $-(O-$ or $-O\ R_8)-$, thio $-(S-)$, cycloalkyls, propanones $-(C=O)-CR_8=CR_9-$, sulfonamides $-(NR_8-(S=O)_2)-$, and sulfonates $-(O-(S=O)_2)-$; wherein R_8 , R_9 , R_{10} , or R_{11}
- 25 are alternatively H, alkyl, amino, amido, cyano, hydroxyl, or carboxy;
- provided that said compound is not combretastatin A1 or a salt, ester, or prodrug thereof.
5. A compound comprising a quinone, quinone prodrug, or a pharmaceutically acceptable salt form thereof having one of the following general structures: /



or



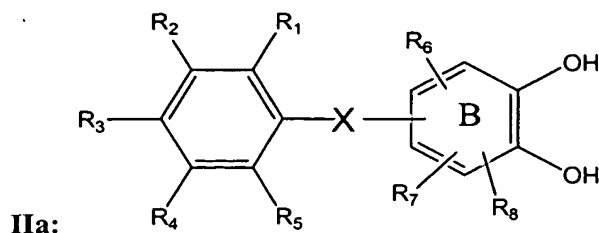
wherein:

- a. at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , or R_8 are the same or different and are optionally selected from
 - i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - iii) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;
 - v) NH_2 , or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido;
 - vi) an oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;

and the remaining R₁, R₂, R₃, R₄, R₅, R₆, R₇, or R₈ are H; and

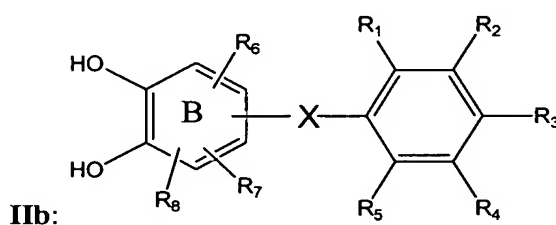
- b. X is selected from the group consisting of alkenes (-CR₉=CR₁₀-), alkanes (-CR₉-CR₁₁R₁₂), alkynes, amides (-NR₉-CO-), amines (-NH-, -NR₈-, or -CR₉-N-), carbonyl (-CO-), ethers (-C R₈-O-), sulfonamides (-NR₈-SO₂-), sulfonates (-O-SO₂-), aryls, oxo (-O- or -O R₈-), thio (-S-) cycloalkyls, propanones (-(C=O)-CR₈=CR₉-), sulfonamides (-NR₈-(S=O)₂-), and sulfonates (-O-(S=O)₂-); wherein R₈, R₉, R₁₀, or R₁₁ are alternatively H, alkyl, amino, amido, cyano, hydroxyl, or carboxy.
6. The compound of claim 5, wherein X forms a covalent linkage between Ring A and B comprising two contiguous atoms of the same or different element.
7. The compound of claim 6, wherein the covalent linkage is an ethylene group (-CH=CH-) and Rings A and B are in a cis (Z) isomeric configuration.
8. The compound of claim 7, wherein R₂, R₃, and R₄ are methoxy.
9. The compound of claim 5, wherein said quinone is a bioreductive agent which is reductively activated *in vivo* to form a catechol capable of participating in a redox cycling reaction to form one or more Reactive Oxygen Species ("ROS").

10. A compound comprising a catechol, catechol prodrug, or a pharmaceutically acceptable salt form thereof having one of the following general structures:



5

or



wherein:

- a. at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , or R_8 are the same or different and are selected from
- i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - iii) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;
 - v) NH_2 , or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido;

vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, heterocyclo;

and the remaining R₁, R₂, R₃, R₄, R₅, R₆, R₇, or R₈ are H; and

- 5 b. X is selected from the group consisting of alkenes (-CR₉=CR₁₀-), alkanes (-CR₉-CR₁₀R₁₁), alkynes, amides (-NR₉-CO-), amines (-NH-, -NR₉-, or -CR₉-N-), carbonyl (-CO-), ethers (-C R₉-O-), sulfonamides (-NR₉-SO₂-), sulfonates (-O-SO₂-), aryls, oxo (-O- or -O R₉-), thio (-S-) cycloalkyls, propanones (-C(=O)-CR₉=CR₁₀-), sulfonamides (-NR₉-(S=O)₂-), and sulfonates (-O-(S=O)₂-);
10 wherein R₉, R₁₀, or R₁₁ are alternatively H, alkyl, amino, amido, cyano, hydroxyl, or carboxy;

provided that said compound is not combretastatin A1 or a salt, ester, or prodrug thereof.

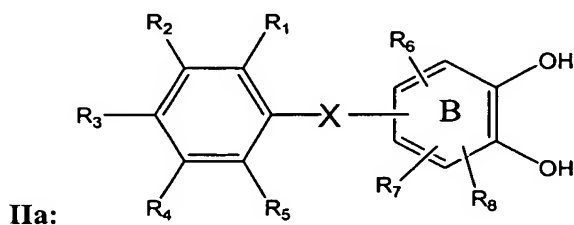
11. The compound of claim 10, wherein X forms a covalent linkage between Ring A and B, comprising two contiguous atoms of the same or different element.
12. The compound of claim 11, wherein the covalent linkage is an ethylene group (-CH=CH-), and Rings A and B are in a cis (Z) isomeric configuration.
15
13. The compound of claim 12, wherein R₂, R₃, and R₄ are methoxy.
14. The compound of claim 13, wherein R₈ is selected from
- i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - 20 ii) a halogen or trihaloalkyl;
 - iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 - 25 v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido;

- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;

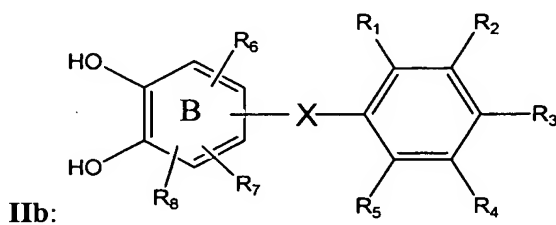
and the remaining R₁, R₅, R₆ and R₇ are H.

- 5 15. The compound of claim 14, wherein R₈ is OH or -O-CH₂-CH=CH₂.
16. The compound of claim 4, wherein said catechol is a biooxidative agent which is oxidatively activated *in vivo* to form a quinone capable of participating in a redox cycling reaction to form one or more Reactive Oxygen Species ("ROS").
- 10 17. A method of inhibiting the proliferation of tumor cells, comprising administering to a mammal an antiproliferative agent capable of forming a Reactive Oxygen Species.
18. A method of inhibiting the proliferation of tumor cells, comprising administering to a mammal a composition which selectively reduces blood flow to a tumor region and forms a ROS *in vivo*, wherein said composition comprises an anticancer agent having a quinone, quinone prodrug, catechol or catechol prodrug moiety.
- 15 19. The method of claim 18, wherein said reduced tumor blood flow is reversible.

20. A method of inhibiting the proliferation of tumor cells, comprising administering to a mammal a catechol, catechol prodrug, or a pharmaceutically acceptable salt form thereof having one the following general structures:



or



wherein:

- 10 a. at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , or R_8 are the same or different and are optionally selected from
 - i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - 15 iii) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;
 - v) NH_2 , or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido,

20 lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or

- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;

and the remaining R₁, R₂, R₃, R₄, R₅, R₆, R₇, or R₈ are H; and

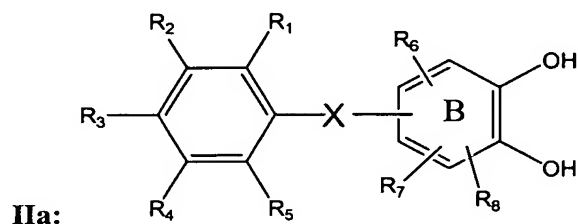
- 5 b. X is selected from the group consisting of alkenes (-CR₉=CR₁₀-), alkanes (-CR₉-CR₁₀R₁₁), alkynes, amides (-NR₉-CO-), amines (-NH-, -NR₉-, or -CR₉-N-), carbonyl (-CO-), ethers (-C R₉-O-), sulfonamides (-NR₉-SO₂-), sulfonates (-O-SO₂-), aryls, oxo (-O- or -O R₉-), thio (-S-) cycloalkyls, propanones (-C(=O)-CR₉=CR₁₀-), sulfonamides (-NR₉-(S=O)₂-), and sulfonates (-O-(S=O)₂-);
 10 wherein R₉, R₁₀, or R₁₁ are alternatively H, alkyl, amino, amido, cyano, hydroxyl, or carboxy.

21. The method of claim 20, wherein X forms a covalent linkage between Ring A and B comprised of two contiguous atoms of the same or different element.
22. The method of claim 21, wherein the covalent linkage is an ethylene group (-CH=CH-) and Rings A and B are in a cis (Z) isomeric configuration.
- 15 23. The method of claim 22, wherein R₂, R₃, and R₄ are methoxy.
24. The method of claim 23, wherein R₈ is selected from
- i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;
- 20 iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, vinyloxy;
- iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
- v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or
- 25 aralkanoylamido; and
- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; or

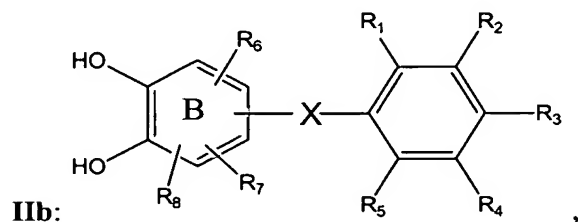
and the remaining R_1 , R_5 , R_6 and R_7 are H.

25. The method of claim 24, wherein R_8 is OH or $-O-CH_2-CH=CH_2$.

26. A method of reducing blood flow in a patient suffering from a vascular proliferative disorder, comprising administering to the patient an effective amount of a catechol, catechol prodrug, or a pharmaceutically acceptable salt form thereof of one the following general structures:



or



wherein:

a. at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , or R_8 are the same or different and are optionally selected from

- i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;
- iii) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
- iv) OH, or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;

- v) NH_2 , or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
- 5 vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;
- and the remaining R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , or R_8 are H; and
- b. X is selected from the group consisting of alkenes ($-\text{CR}_9=\text{CR}_{10}-$), alkanes ($-\text{CR}_9-\text{CR}_{10}\text{R}_{11}$), alkynes, amides ($-\text{NR}_9-\text{CO}-$), amines ($-\text{NH}-$, $-\text{NR}_9-$, or $-\text{CR}_9-\text{N}-$), carbonyl ($-\text{CO}-$), ethers ($-\text{C R}_9-\text{O}-$), sulfonamides ($-\text{NR}_9-\text{SO}_2-$), sulfonates ($-\text{O}-\text{SO}_2-$), aryls, oxo ($-\text{O}-$ or $-\text{O R}_9-$), thio ($-\text{S}-$) cycloalkyls, propanones ($-(\text{C}=\text{O})-\text{CR}_9=\text{CR}_{10}-$), sulfonamides ($-\text{NR}_9-(\text{S}=\text{O})_2-$), and sulfonates ($-\text{O}-(\text{S}=\text{O})_2-$); wherein R_9 , R_{10} , or R_{11} are alternatively H, alkyl, amino, amido, cyano, hydroxyl, or carboxy.
- 10
- 15 27. The method of claim 26, wherein X forms a covalent linkage between Ring A and B comprised of two contiguous atoms of the same or different element.
28. The method of claim 27, wherein the covalent linkage is an ethylene group ($-\text{CH}=\text{CH}-$) and Rings A and B are in a cis (Z) isomeric configuration.
29. The method of claim 28, wherein R_2 , R_3 , and R_4 are methoxy.
- 20 30. The method of claim 29, wherein R_8 is selected from
- i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;
- iii) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
- 25 iv) OH , or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;
- v) NH_2 , amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido,

arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or

- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;

5 and the remaining R_1 , R_5 , R_6 and R_7 are H.

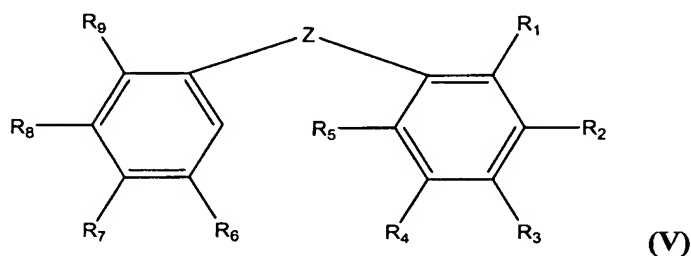
31. The method of claim 30, wherein R_8 is OH or $-O-CH_2-CH=CH_2$.

32. The method of claim 26, wherein said vascular proliferative disorder is selected from the group consisting of solid tumor cancer, wet age-related macular degeneration, diabetic retinopathy, retinopathy of prematurity, diabetic macular edema, uveitis, corneal neovascularization, psoriasis, rheumatoid arthritis, atheroma, restenosis, Kaposi's sarcoma, haemangioma, and inflammatory diseases characterized by vascular proliferation.

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33. The method of claim 26, wherein the blood flow reduction causes the occlusion, destruction, or damage of proliferating vasculature.

34. A composition of the following formula (V):



15

wherein

- a. Z is an ethylene ($-CH=CH-$) bridge in the cis (Z) isomeric configuration;
- b. R_1 and R_2 are OH or a prodrug form thereof;
- c. at least one of R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , and R_9 are optionally

20

- i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;

- 5 iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino,
 10 heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, aralkanoylamido; or
 vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
 15 the remaining R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are hydrogen.

35. The composition of claim 34, wherein at least three of R₆, R₇, R₈, and R₉ are not hydrogen.

36. The composition of claim 35, wherein R₆, R₇, and R₈ are the same.

15 37. The composition of claim 36, wherein R₆, R₇, and R₈ are methoxy.

38. The composition of claim 37, wherein R₃ is

- i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 ii) a halogen or trihaloalkyl;
 20 iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido,
 25 arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
 vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
 R₄, R₅, and R₉ are hydrogen.

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39. The composition of claim 38, wherein R₃ is -CH₃, -CH₂CH₃, -OCH₂CH₃, -F, -Br, -CF₃, -CBr₃, -OH, -O-CH₂-CH=CH₂, -CH₂-CH₂=CH₂, -NH₂, -NO₂, -cyano, -carboxy, or -benzyl.

40. The composition of claim 39, wherein R₆, R₇, and R₈ are F.

5 41. The composition of claim 40, wherein R₃ is

- i) a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;
- 10 iii) a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
- iv) OH, or a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) primary, secondary, or tertiary alcohol;
- v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, 15 arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and

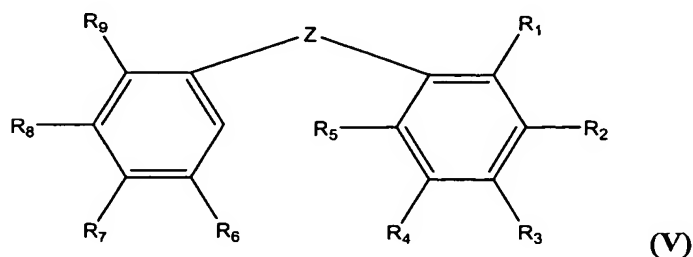
R₄, R₅, and R₉ are hydrogen.

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42. The composition of claim 41, wherein R₃ is -CH₃, -CH₂CH₃, -OCH₂CH₃, -F, -Br, -CF₃, -CBr₃, -OH, -O-CH₂-CH=CH₂, -CH₂-CH₂=CH₂, -NH₂, -NO₂, -cyano, -carboxy, or -benzyl.

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43. A method of inhibiting the proliferation of tumor cells, comprising administering to a mammal a catechol, catechol prodrug, or a pharmaceutically acceptable salt form thereof of formula (V):



5 wherein

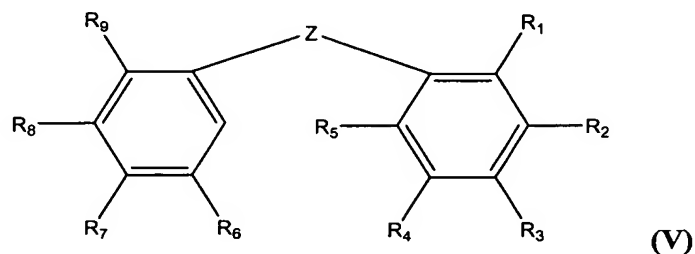
- a. Z is an ethylene (-CH=CH-) bridge in the cis (Z) isomeric configuration;
 - b. R₁ and R₂ are OH or a prodrug form thereof;
 - c. at least one of R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are optionally
 - i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 - 15 v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
 - vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
 - d. the remaining R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are hydrogen.
44. The method of claim 43, wherein at least three of R₆, R₇, R₈, and R₉ are not hydrogen.
45. The method of claim 44, wherein R₆, R₇, and R₈ are the same.
46. The method of claim 45, wherein R₆, R₇, and R₈ are methoxy.

47. The method of claim 46, wherein R₃ is

- i) a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - 5 iii) a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) primary, secondary, or tertiary alcohol;
 - v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
 - 10 vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
- 15 R₄, R₅, and R₉ are hydrogen.

48. The method of claim 47, wherein R₃ is -CH₃, -CH₂CH₃, -OCH₂CH₃, -F, -Br, -CF₃, -CBr₃, -OH, -O-CH₂-CH=CH₂, -CH₂-CH₂=CH₂, -NH₂, -NO₂, -cyano, -carboxy, or -benzyl.

20 49. A method of reducing blood flow in a patient suffering from a vascular proliferative disorder, comprising administering to the patient an effective amount of a catechol, catechol prodrug, or a pharmaceutically acceptable salt form thereof of formula (V):



wherein

- a. Z is an ethylene (-CH=CH-) bridge in the cis (Z) isomeric configuration;

- b. R₁ and R₂ are OH or a prodrug form thereof;
- c. at least one of R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are optionally
- i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - 5 ii) a halogen or trihaloalkyl;
 - iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 - v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
 - 10 vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
- d. the remaining R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are hydrogen.
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50. The method of claim 49, wherein at least three of R₆, R₇, R₈, and R₉ are not hydrogen.
51. The method of claim 50, wherein R₆, R₇, and R₈ are the same.
52. The method of claim 51, wherein R₆, R₇, and R₈ are methoxy.
53. The method of claim 52, wherein R₃ is
- 20 i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - 25 iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 - v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or

vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and

R₄, R₅, and R₉ are hydrogen.

- 5 54. The method of claim 53, wherein R₃ is -CH₃, -CH₂CH₃, -OCH₂CH₃, -F, -Br, -CF₃, -CBr₃, -OH, -O-CH₂-CH=CH₂, -CH₂-CH₂=CH₂, -NH₂, -NO₂, -cyano, -carboxy, or -benzyl.
55. The method of claim 49, wherein said vascular proliferative disorder is selected from the group consisting of solid tumor cancer, wet age-related macular degeneration, diabetic retinopathy, retinopathy of prematurity, diabetic macular edema, uveitis, corneal neovascularization, psoriasis, rheumatoid arthritis, atheroma, restenosis, Kaposi's sarcoma, haemangioma, and inflammatory diseases characterized by vascular proliferation.
- 10 56. The method of claim 49, wherein the reduction in blood flow causes the occlusion, destruction, or damage of proliferating vasculature.
- 15 57. A composition selected from the group consisting of 6-[(Z)-2-(3,4,5-Trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 3-Ethyl-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene 3-Methyl-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 4-Bromo-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 4-Phenyl-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 3-Allyl-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 4-Fluoro-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 2,3,4-Trihydroxy-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-benzene, 2,3-Dihydroxy-4-ethoxy-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-benzene, 2,3-Dihydroxy-4-allyloxy-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-benzene, 4-Nitro-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-2,3-dihydroxybenzene, 2',3'dihydroxy-3,5-dichloro-4,4'-dimethoxy-(Z)-stilbene, 2',3'dihydroxy-4'-methoxy-3,4,5-trifluoro-(Z)-stilbene, 2,3-Dihydroxy-4-methoxy-[(Z)-2-(3,4,5-trimethoxyphenyl) Beta lactam]-benzene, 2',3' diphosphate-3,4,5-trimethoxy-(Z)-stilbene, tetrasodium salt; 3',4' diphosphate-3,4,5-trimethoxy-(Z)-stilbene, tetrasodium salt; and combinations thereof.
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